Abstract

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Title of candidate thesis: Alkylamino- derivatives of pyrazinamide as potential antituberculotic drugs

This thesis is a result of intention to prepare potential effective derivatives from pyrazinamide (PZA) structure. These results contribute to enrichment of the research of new antituberculars (antiTBC) which has been carried out at the Dpt. of Pharmaceutical Chemistry and Drug Control at the Faculty of Pharmacy in Hradec Králové.

The aim of the research to produce the new effective antituberculars is supported by the contemporary state of tuberculosis in the world. This state is closely described in this thesis. Despite of decreasing number of new cases in all six WHO regions, spreading of this infectious disease is not under the control. The main reason is a resistance formation of new mycobacterial strains which can cause hardly treatable cases. The prepared substances are PZA derivatives which represent one of the most important first line drugs for tuberculosis treatment. The latest research focused on mechanism of PZA showed new information which was included in this thesis.

Furthermore, some new systems for delivery of antiTBCs are presented here. They involve inhalation systems and just this administration of drugs can make treatment of this disease more effective. It includes inhalation systems, an effective way of drug administration. Promising results were shown during the testing on animals.

As a part of this thesis, 12 new PZA derivatives were prepared. It includes a series of 5-(alkylamino)-*N*-phenylpyrazine-2-carboxamides and 5-(alkylamino)-*N*-(2-chlorophenyl)pyrazine-2-carboxamides. The prepared compounds were characterized by melting points, mass spectra, ^{1}H a ^{13}C NMR and infrared spectra. The compounds were evaluated for antimycobacterial activity (*Mycobacterium tuberculosis*, *M. kansasii a* two stems of *M. avium*), and in addition also for activity against selected bacterial and fungal pathogens. 5-(Alkylamino)-*N*-phenylpyrazine-2-carboxamides inhibited the growth of *M. tuberculosis* at concentrations of 0,78 – 3,13 $\mu g.mL^{-1}$, which was superior to PZA standard.